The Body's Defenses

If microorganisms never encountered resistance from our body defenses, we would be constantly ill and would eventually die of various diseases. Fortunately, in most cases our defenses prevent this from happening. Some of these defenses are designed to keep microorganisms from entering the body. Other defenses remove the microorganisms if they manage to get inside. Further defenses attack the microorganisms if they remain inside the body. The ability to ward off disease through the various defense mechanisms is called **resistance**. The lack of resistance, or vulnerability to disease, is known as **susceptibility**. One form of defense is referred to as **non-specific resistance**, and includes defenses that protect us from any pathogen. This includes a first line of defense such as the physical barriers to infection (skin and mucous membranes) and a second line of defense (phagocytes, inflammation, fever, and antimicrobial substances). **Specific resistance** is a third line of defense that forms the **immune response** and targets specific pathogens. Specialized cells of the immune system, called lymphocytes, produce specific proteins called antibodies which are produced against specific antigens.

1st Line of Defense

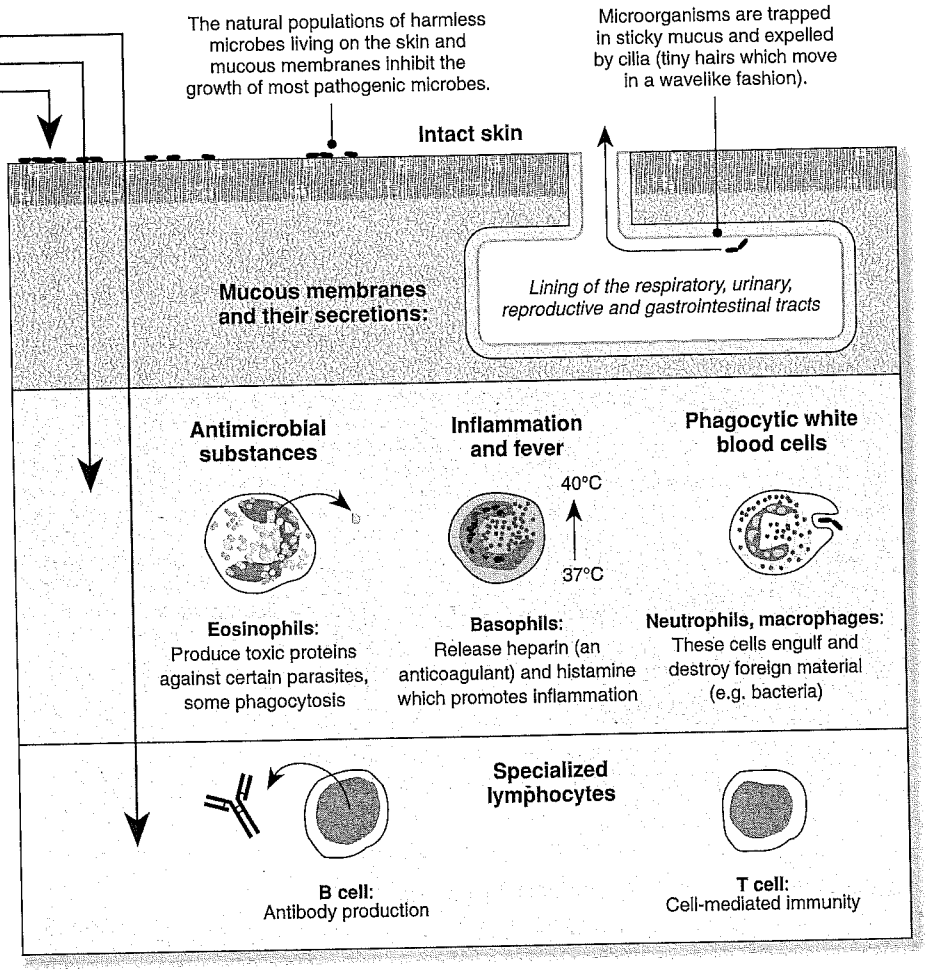
The skin provides a formidable physical barrier to the entry of pathogens. Healthy skin is rarely penetrated by microorganisms. Certain chemical secretions are produced by skin that inhibit growth of bacteria and fungi. Tears, mucus, and saliva also help to wash bacteria away.

2nd Line of Defense

A range of defense mechanisms operate inside the body to inhibit or destroy pathogens. These responses react to the presence of any pathogen, regardless of which species it is. White blood cells are involved in most of these responses.

3rd Line of Defense

Once the pathogen has been identified by the immune system, a **specific response** from white blood cells called lymphocytes occurs. Lymphocytes coordinate a range of specific responses to the pathogen.



1. Compare and contrast the type of response against pathogens carried out by each of the three levels of defense:

2. Distinguish between specific and non-specific resistance: _____

3. Describe features of the different types of white blood cells and explain how these relate to their role in the second line of defense:

4. Describe the functional role of each of the following defense mechanisms (the first one has been completed for you):

(a) Skin (including sweat and sebum production): Skin helps to prevent direct entry of pathogens into the body. Sebum slows growth of bacteria and fungi.

(b) Phagocytosis by white blood cells: _____

(c) Mucus-secreting and ciliated membranes: _____

(d) Body secretions: tears, urine, saliva, gastric juice: _____

(e) Natural antimicrobial proteins (e.g. interferon): _____

(f) Antibody production: _____

(g) Fever: _____

(h) Cell-mediated immunity: _____

(i) The inflammatory response: _____

5. Infection with HIV results in the progressive destruction of T lymphocytes. Suggest why this leads to an increasing number of opportunistic infections in AIDS sufferers:

The Lymphatic System

Fluid leaks out from capillaries and forms the tissue fluid, which is similar in composition to plasma but lacks large proteins. This fluid bathes the tissues, supplying them with nutrients and oxygen, and removing wastes. Some of the tissue fluid returns directly into the capillaries, but some drains back into the blood circulation through a network of lymph vessels. This fluid, called **lymph**, is similar to tissue fluid, but contains more leukocytes. Apart from its circulatory role, the lymphatic system also has an important function in the immune response. Lymph nodes are the primary sites where the destruction of pathogens and other foreign substances occurs. A lymph node that is fighting an infection becomes swollen and hard as the lymph cells reproduce rapidly to increase their numbers. The thymus, spleen, and bone marrow also contribute leukocytes to the lymphatic and circulatory systems.

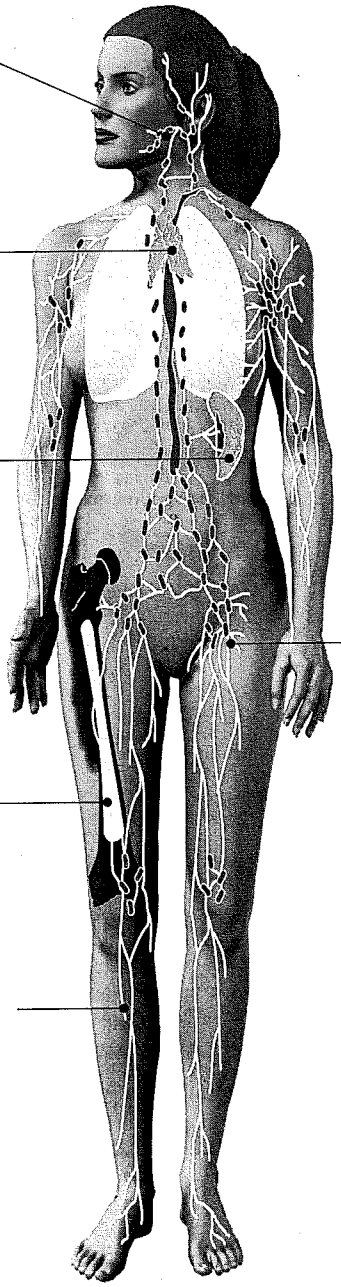
Tonsils: Tonsils (and adenoids) comprise a collection of large lymphatic nodules at the back of the throat. They produce lymphocytes and antibodies and are well-placed to protect against invasion of pathogens.

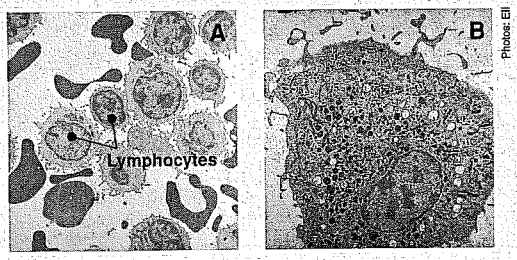
Thymus gland: The thymus is a two-lobed organ located close to the heart. It is prominent in infants and diminishes after puberty to a fraction of its original size. Its role in immunity is to help produce **T cells** that destroy invading microbes directly or indirectly by producing various substances.

Spleen: The oval spleen is the largest mass of lymphatic tissue in the body, measuring about 12 cm in length. It stores and releases blood in case of demand (e.g. in cases of bleeding), produces mature **B cells**, and destroys bacteria by phagocytosis.

Bone marrow: Bone marrow produces red blood cells and many kinds of leukocytes: monocytes (and macrophages), neutrophils, eosinophils, basophils, and lymphocytes (B cells and T cells).

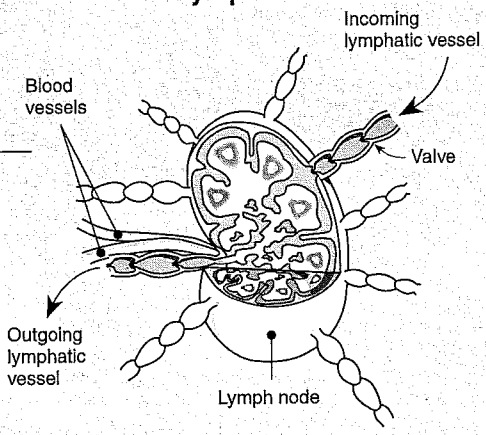
Lymphatic vessels: When tissue fluid is picked up by lymph capillaries, it is called **lymph.** The lymph is passed along lymphatic vessels to a series of lymph nodes. These vessels contain one-way valves that move the lymph in the direction of the heart until it is reintroduced to the blood at the subclavian veins.





Many types of leukocytes are involved in internal defense. The photos above illustrate examples of leukocytes. **A** shows a cluster of **lymphocytes. B** shows a single **macrophage:** large, phagocytic cells that develop from monocytes and move from the blood to reside in many organs and tissues, including the spleen and lymph nodes.

Lymph node



Lymph nodes are oval or bean-shaped structures, scattered throughout the body, usually in groups, along the length of lymphatic vessels. As lymph passes through the nodes, it filters foreign particles (including pathogens) by trapping them in fibers. Lymph nodes are also a "store" of **lymphocytes**, which may circulate to other parts of the body. Once trapped, macrophages destroy the foreign substances by phagocytosis. T cells may destroy them by releasing various products, and/or B cells may release antibodies that destroy them.

1. Briefly describe the composition of lymph: _____

_____

2. Discuss the various roles of lymph: _____

_____

_____

3. Describe one role of each of the following in the lymphatic system:

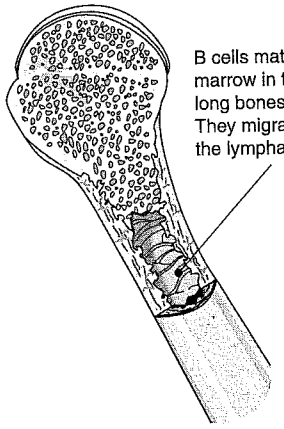
(a) Lymph nodes: _____

(b) Bone marrow: _____

The Immune System

The efficient internal defense provided by the immune system is based on its ability to respond specifically against a foreign substance and its ability to hold a memory of this response. There are two main components of the immune system: the humoral and the cell-mediated responses. They work separately and together to protect us from disease. The **humoral immune response** is associated with the serum (non-cellular part of the blood) and involves the action of **antibodies** secreted by B cell lymphocytes. Antibodies are found in extracellular fluids including lymph, plasma, and mucus secretions. The humoral response protects the body against circulating viruses, and bacteria and their toxins. The **cell-mediated immune response** is associated with the production of specialized lymphocytes called **T cells**. It is most effective against bacteria and viruses located within host cells, as well as against parasitic protozoa, fungi, and worms. This system is also an important defense against cancer, and is responsible for the rejection of transplanted tissue. Both B and T cells develop from stem cells located in the liver of fetuses and the bone marrow of adults. T cells complete their development in the thymus, whilst the B cells mature in the bone marrow.

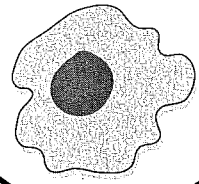
Lymphocytes and their Functions



B cells mature in the bone marrow in the shaft of the long bones (e.g. the femur). They migrate from here to the lymphatic organs.

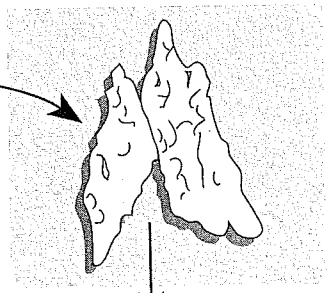
Stem cell

Stem cells in the bone marrow and fetal liver give rise to T cells and B cells.

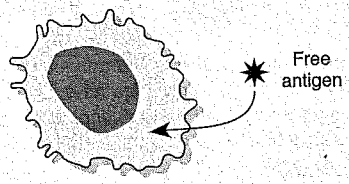


Thymus gland

The thymus gland is located above the heart on the wind pipe. It is large in infants but regresses with age. Immature T cells move to the thymus to mature before migrating to other lymphatic organs.

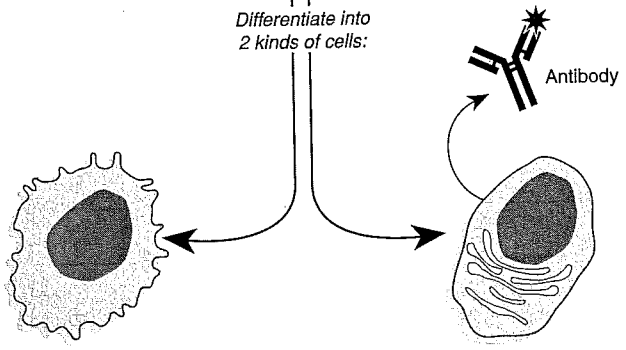


B cell



B cells recognize and bind antigens. Each B cell recognizes one specific antigen. Helper T cells recognize specific antigens on B cell surfaces and induce their maturation and proliferation. A mature B cell may carry as many as 100 000 antigenic receptors embedded in its surface membrane. B cells defend against bacteria and viruses outside the cell and toxins produced by bacteria (free antigens).

Differentiate into 2 kinds of cells:



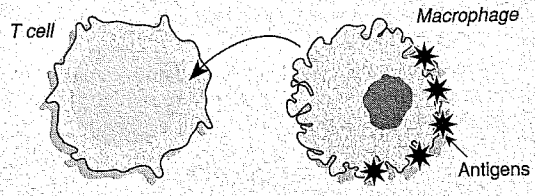
Memory cells

Some B cells differentiate into long-lived memory cells (see opposite). When these cells encounter the same antigen again (even years or decades later), they rapidly differentiate into antibody-producing plasma cells.

Plasma cells

When stimulated by an antigen (see *Clonal Selection*, opposite), some B cells differentiate into plasma cells, which secrete antibodies into the blood system. The antibodies then inactivate the circulating antigens.

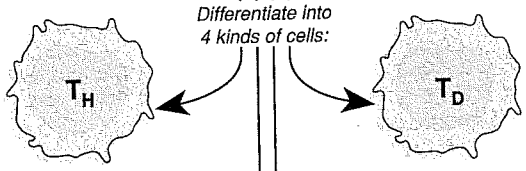
T cell



T cells respond only to antigen fragments that have been processed and presented by infected cells or macrophages (phagocytic cells). They defend against:

- Intracellular bacteria and viruses
- Protozoa, fungi, flatworms, and roundworms
- Cancerous cells and transplanted foreign tissue

Differentiate into 4 kinds of cells:

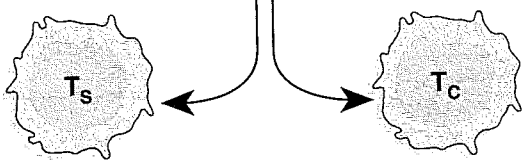


Helper T cell

Activates cytotoxic T cells and other helper T cells. They are necessary for B cell activation.

T cell for delayed hypersensitivity

Protects against pathogens. Causes transplant rejection and inflammation in allergic reactions.



Suppressor T cell

Regulates immune response by turning it off when no more antigen is present.

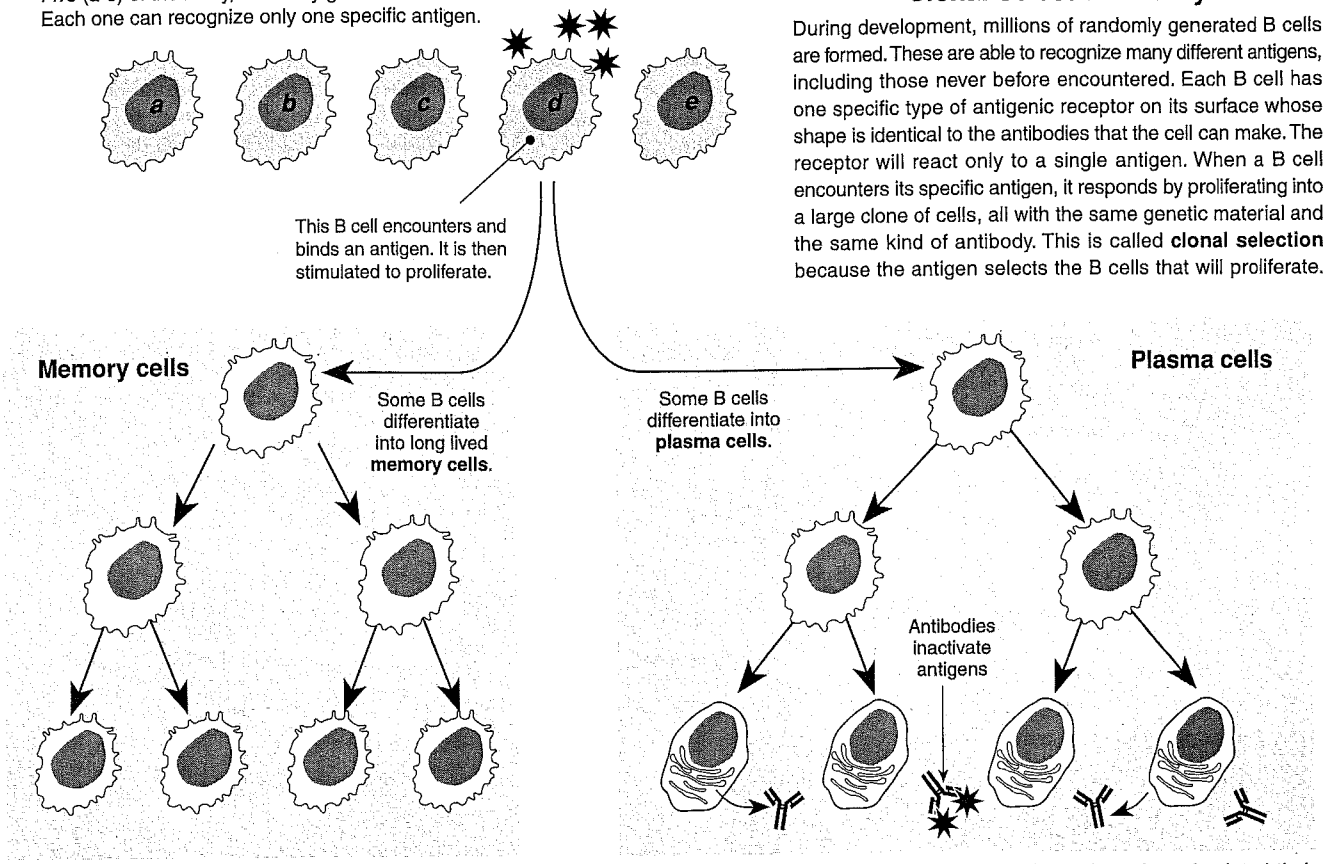
Cytotoxic T cell

Destroys target cells on contact. Recognizes tumor (cancer) or virus infected cells by their surface (antigens and MHC markers).

The immune system has the ability to respond to the large and unpredictable range of potential antigens encountered in the environment. The diagram below explains how this ability is based on **clonal selection** after antigen exposure. The example illustrated is for B cell lymphocytes. In the same way, a T cell stimulated by a specific antigen will multiply and develop into different types of T cells. Clonal selection and differentiation of lymphocytes provide the basis for **immunological memory**.

Clonal Selection Theory

During development, millions of randomly generated B cells are formed. These are able to recognize many different antigens, including those never before encountered. Each B cell has one specific type of antigenic receptor on its surface whose shape is identical to the antibodies that the cell can make. The receptor will react only to a single antigen. When a B cell encounters its specific antigen, it responds by proliferating into a large clone of cells, all with the same genetic material and the same kind of antibody. This is called **clonal selection** because the antigen selects the B cells that will proliferate.



Some B cells differentiate into long lived **memory cells**. These are retained in the lymph nodes to provide future immunity (**immunological memory**). In the event of a second infection, B-memory cells react more quickly and vigorously than the initial B-cell reaction to the first infection.

Plasma cells secrete antibodies specific to the antigen that stimulated their development. Each plasma cell lives for only a few days, but can produce about 2000 antibody molecules per second. Note that during development, any B cells that react to the body's own antigens are selectively destroyed in a process that leads to **self tolerance** (acceptance of the body's own tissues).

1. State the general action of the two major divisions in the immune system:

   (a) Humoral immune system: _____

   (b) Cell-mediated immune system: _____

2. Identify the origin of B cells and T cells (before maturing): _____

3. (a) State where B cells mature: _____ (b) State where T cells mature: _____

4. Briefly describe the function of each of the following cells in the immune system response:

   (a) Memory cells: _____

   (b) Plasma cells: _____

   (c) Helper T cells: _____

   (d) Suppressor T cells: _____

   (e) Delayed hypersensitivity T cells: _____

   (f) Cytotoxic T cells: _____

5. Explain the basis of **immunological memory**: _____

   _____

   _____

   _____